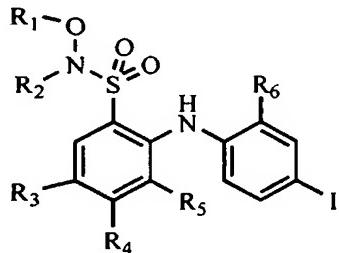


## CLAIMS

1. A method for treating chronic pain, said method comprising administering to a subject in need of such treatment a composition comprising a MEK inhibitor selected from: a compound of formula (I):

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(I)

- R<sub>1</sub> is H, C <sub>1-8</sub> alkyl, C <sub>3-8</sub> alkenyl, C <sub>3-8</sub> alkynyl, C <sub>3-8</sub> cycloalkyl, phenyl, (phenyl)C <sub>1-4</sub> alkyl, (phenyl)C <sub>3-4</sub> alkenyl, (phenyl)C <sub>3-4</sub> alkynyl, (C <sub>3-8</sub> cycloalkyl)-C <sub>1-4</sub> alkyl, (C <sub>3-8</sub> cycloalkyl)C <sub>3-4</sub> alkenyl, (C <sub>3-8</sub> cycloalkyl)C <sub>3-4</sub> alkynyl, C <sub>3-8</sub> heterocyclic radical, (C <sub>3-8</sub> heterocyclic radical)C <sub>1-4</sub> alkyl, (C <sub>3-8</sub> heterocyclic radical)C <sub>3-4</sub> alkenyl, (C <sub>3-8</sub> heterocyclic radical)C <sub>3-4</sub> alkynyl, (CH<sub>2</sub>)<sub>2-4</sub> OR<sub>C</sub> or (CH<sub>2</sub>)<sub>2-4</sub> NR<sub>C</sub>R<sub>D</sub>;

15

R<sub>2</sub> is H, C <sub>1-4</sub> alkyl, phenyl, C <sub>3-6</sub> cycloalkyl, C <sub>3-6</sub> heterocyclic radical, or (C <sub>3-6</sub> cycloalkyl) methyl;

each of R<sub>3</sub> and R<sub>4</sub> is independently selected from H, F, NO<sub>2</sub>, Br and Cl;

20

R<sub>5</sub> is selected from H and F;

R<sub>6</sub> is H, F, Cl or CH<sub>3</sub>;

- 25 each of R<sub>C</sub> and R<sub>D</sub> is independently selected from H, C <sub>1-4</sub> alkyl, C <sub>3-4</sub> alkenyl, C <sub>3-4</sub> alkynyl, C <sub>3-6</sub> cycloalkyl, and phenyl; or NR<sub>C</sub>R<sub>D</sub> may be a piperidino, morpholino, or N-(C <sub>1-6</sub> alkyl)piperazino ring;

wherein each hydrocarbon radical above is optionally substituted with between 1 and 3 substituents independently selected from halo, hydroxyl, amino, (amino)sulfonyl, and NO<sub>2</sub>; and

- 5    wherein each heterocyclic radical above is optionally substituted with between 1 and 3 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>3-6</sub> cycloalkyl, C<sub>3-4</sub> alkenyl, C<sub>3-4</sub> alkynyl, phenyl, hydroxyl, amino, (amino)sulfonyl, and NO<sub>2</sub>, wherein each substituent alkyl, cycloalkyl, alkenyl, alkynyl or phenyl is in turn optionally substituted with between 1 and 2  
10    substituents independently selected from halo, C<sub>1-2</sub> alkyl, hydroxyl, amino, and NO<sub>2</sub>;

or a pharmaceutically acceptable salt or C<sub>1-8</sub> ester thereof.

15

2.    The method of claim 1, wherein said chronic pain is selected from neuropathic pain, idiopathic pain, and pain associated with chronic alcoholism, vitamin deficiency, uremia, or hypothyroidism.

20    3.    The method of claim 2, wherein said chronic pain is a type of neuropathic pain.

25    4.    The method of claim 3, wherein said neuropathic pain is associated with one of the following: inflammation, postoperative pain, phantom limb pain, burn pain, gout, trigeminal neuralgia, acute herpetic and postherpetic pain, causalgia, diabetic neuropathy, plexus avulsion, neuroma, vasculitis, viral infection, crush injury, constriction injury, tissue injury, limb amputation, post-operative pain, arthritis pain, and any other nerve injury between the peripheral nervous system and the central nervous system, inclusively.

30    5.    The method of claim 2, wherein said chronic pain is associated with chronic alcoholism, vitamin deficiency, uremia, or hypothyroidism.

6. The method of claim 2, wherein said chronic pain is associated with idiopathic pain.

5 7. The method of claim 1, wherein said chronic pain is associated with inflammation.

8. The method of claim 1, wherein said chronic pain is associated with arthritis.

10

9. The method of claim 1, wherein said chronic pain is associated with post-operative pain.

15 10. The method of claim 1, wherein R<sub>3</sub> is bromo or chloro.

11. The method of claim 1, wherein R<sub>4</sub> is fluoro.

12. The method of claim 1, wherein R<sub>5</sub> is H.

20

13. The method of claim 12, wherein each of R<sub>4</sub> and R<sub>5</sub> is H.

14. The method of claim 1, wherein each of R<sub>4</sub> and R<sub>5</sub> is fluoro.

25 15. The method of claim 14, wherein R<sub>3</sub> is bromo.

16. The method of claim 14, wherein R<sub>3</sub> is fluoro.

17. The method of claim 1, wherein R<sub>4</sub> is nitro.

30

18. The method of claim 16, wherein R<sub>5</sub> is H.

19. The method of claim 1, wherein R<sub>6</sub> is chloro.

20. The method of claim 1, wherein R<sub>6</sub> is methyl.

5 21. The method of claim 1, wherein R<sub>1</sub> is H or C<sub>1-4</sub> alkyl, and R<sub>2</sub> is H.

22. The method of claim 1, wherein R<sub>1</sub> is (C<sub>3-6</sub> cycloalkyl)methyl.

23. The method of claim 1, wherein R<sub>1</sub> is H.

10

24. The method of claim 1, wherein R<sub>1</sub> is (CH<sub>2</sub>)<sub>2-4</sub>OR<sub>C</sub> or (CH<sub>2</sub>)<sub>2-4</sub>NR<sub>C</sub>R<sub>D</sub>.

25. The method of claim 1, wherein said MEK inhibitor has a structure selected from: 4-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzenesulfonic acid; 4-fluoro-N-hydroxy-2-(4-iodo-2-methyl-phenylamino)-

15 benzenesulfonamide; N-cyclopropylmethoxy-4-fluoro-2-(4-iodo-2-methyl-phenylamino)-benzenesulfonamide; 3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzenesulfonic acid; 3,4-difluoro-N-hydroxy-2-(4-iodo-2-methyl-phenylamino)-benzenesulfonamide; N-cyclopropylmethoxy-3,4-

20 difluoro-2-(4-iodo-2-methyl-phenylamino)-benzenesulfonamide; 3,4,5-trifluoro-2-(4-iodo-2-methyl-phenylamino)-benzenesulfonic acid; 3,4,5-trifluoro-N-

hydroxy-2-(4-iodo-2-methyl-phenylamino)-benzenesulfonamide; N-cyclopropylmethoxy-3,4,5-trifluoro-2-(4-iodo-2-methyl-phenylamino)-

benzenesulfonamide; 5-bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzenesulfonic acid; 5-bromo-3,4-difluoro-N-hydroxy-2-(4-iodo-2-methyl-

25 phenylamino)-benzenesulfonamide; 5-bromo-N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzenesulfonamide; 2-(4-iodo-2-

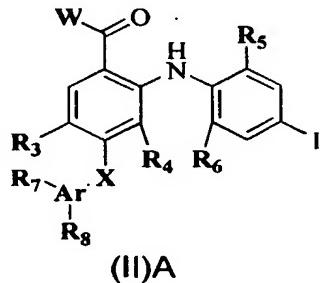
methyl-phenylamino)-4-nitro-benzenesulfonic acid; N-hydroxy-2-(4-iodo-2-methyl-phenylamino)-4-nitro-benzenesulfonamide; and

30 N-cyclopropylmethoxy-2-(4-iodo-2-methyl-phenylamino)-4-nitro-benzenesulfonamide.

26. The method of claim 1, wherein said MEK inhibitor has a structure selected from: 2-(2-chloro-4-iodo-phenylamino)-4-fluoro-benzenesulfonic acid; 2-(2-chloro-4-iodo-phenylamino)-4-fluoro-N-hydroxy-benzenesulfonamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-4-fluoro-benzenesulfonamide; 2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-benzenesulfonic acid; 2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-N-hydroxy-benzenesulfonamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-benzenesulfonamide; 2-(2-chloro-4-iodo-phenylamino)-3,4,5-trifluoro-benzenesulfonic acid; 2-(2-chloro-4-iodo-phenylamino)-3,4,5-trifluoro-N-hydroxy-benzenesulfonamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4,5-trifluoro-benzenesulfonamide; 5-bromo-2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-benzenesulfonic acid; 5-bromo-2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-N-hydroxy-benzenesulfonamide; 5-bromo-2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-benzenesulfonamide; 2-(2-chloro-4-iodo-phenylamino)-4-nitro-benzenesulfonic acid; 2-(2-chloro-4-iodo-phenylamino)-N-hydroxy-4-nitro-benzenesulfonamide; and 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-4-nitro-benzenesulfonamide.

20 27. A method for treating chronic pain, said method comprising administering to a subject in need of such treatment a composition comprising a MEK inhibitor selected from a compound having the formula (II)A:

25



W is OR<sub>1</sub>, NR<sub>2</sub>OR<sub>1</sub>, NR<sub>A</sub>R<sub>B</sub>, NR<sub>2</sub>NR<sub>A</sub>R<sub>B</sub>, or NR<sub>2</sub>(CH<sub>2</sub>)<sub>2-4</sub>NR<sub>A</sub>R<sub>B</sub>;

R<sub>1</sub> is H, C<sub>1-8</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl, C<sub>3-8</sub> cycloalkyl, phenyl, (phenyl)C<sub>1-4</sub> alkyl, (phenyl)C<sub>3-4</sub> alkenyl, (phenyl)C<sub>3-4</sub> alkynyl, (C<sub>3-8</sub>

5 cycloalkyl)-

C<sub>1-4</sub> alkyl, (C<sub>3-8</sub> cycloalkyl)C<sub>3-4</sub> alkenyl, (C<sub>3-8</sub> cycloalkyl)C<sub>3-4</sub> alkynyl, C<sub>3-8</sub> heterocyclic radical, (C<sub>3-8</sub> heterocyclic radical)C<sub>1-4</sub> alkyl, (C<sub>3-8</sub> heterocyclic radical)C<sub>3-4</sub> alkenyl, (C<sub>3-8</sub> heterocyclic radical)C<sub>3-4</sub> alkynyl or (CH<sub>2</sub>)<sub>2-4</sub>NR<sub>A</sub>R<sub>B</sub>;

10 R<sub>2</sub> is H, phenyl, C<sub>1-4</sub> alkyl, C<sub>3-4</sub> alkenyl, C<sub>3-8</sub> alkynyl, C<sub>3-8</sub> cycloalkyl, or (C<sub>3-8</sub> cycloalkyl)-C<sub>1-4</sub> alkyl;

R<sub>A</sub> is H, C<sub>1-6</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl, C<sub>3-8</sub> cycloalkyl, phenyl, (C<sub>3-8</sub> cycloalkyl)C<sub>1-4</sub> alkyl, (C<sub>3-8</sub> cycloalkyl)C<sub>3-4</sub> alkenyl, (C<sub>3-8</sub> cycloalkyl)C<sub>3-4</sub>

15 alkynyl, C<sub>3-8</sub> heterocyclic radical, (C<sub>3-8</sub> heterocyclic radical)C<sub>1-4</sub> alkyl, (aminosulfonyl)phenyl, [(aminosulfonyl)phenyl]C<sub>1-4</sub> alkyl, (aminosulfonyl)C<sub>1-6</sub> alkyl, (aminosulfonyl)C<sub>3-6</sub> cycloalkyl, or [(aminosulfonyl)C<sub>3-6</sub> cycloalkyl]C<sub>1-4</sub> alkyl;

20 R<sub>B</sub> is H, C<sub>1-8</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl, C<sub>3-8</sub> cycloalkyl, or C<sub>6-8</sub> aryl;

R<sub>3</sub> is halo, NO<sub>2</sub>, SO<sub>2</sub>NR<sub>I</sub>(CH<sub>2</sub>)<sub>2-4</sub>NR<sub>E</sub>R<sub>F</sub>, SO<sub>2</sub>NR<sub>I</sub>R<sub>K</sub> or (CO)T;

T is C<sub>1-8</sub> alkyl, C<sub>3-8</sub> cycloalkyl, (NR<sub>E</sub>R<sub>F</sub>)C<sub>1-4</sub> alkyl, OR<sub>F</sub>, NR<sub>I</sub>(CH<sub>2</sub>)<sub>2-4</sub>NR<sub>E</sub>R<sub>F</sub>, or

25 NR<sub>E</sub>R<sub>F</sub>;

R<sub>4</sub> is H or F;

R<sub>5</sub> is H, methyl, halo, or NO<sub>2</sub>;

30

R<sub>6</sub> is H, methyl, halo, or NO<sub>2</sub>;

Ar is phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl;

- each of R<sub>7</sub> and R<sub>8</sub> is independently selected from H, halo, C<sub>1-4</sub> alkyl, SO<sub>2</sub>NR<sub>J</sub>(CH<sub>2</sub>)<sub>2-4</sub>NR<sub>G</sub>R<sub>H</sub>, (CO)(CH<sub>2</sub>)<sub>2-4</sub>NR<sub>G</sub>R<sub>H</sub>, (CO)NR<sub>J</sub>(CH<sub>2</sub>)<sub>2-4</sub>NR<sub>G</sub>R<sub>H</sub>,  
5 (CO)O(CH<sub>2</sub>)<sub>2-4</sub>NR<sub>G</sub>R<sub>H</sub>, SO<sub>2</sub>NR<sub>G</sub>R<sub>H</sub>, and (CO)NR<sub>G</sub>R<sub>H</sub>; provided that where Ar is a pyridyl, each of R<sub>7</sub> and R<sub>8</sub> is H;

- each of R<sub>C</sub>, R<sub>D</sub>, R<sub>E</sub>, R<sub>F</sub>, R<sub>G</sub>, and R<sub>H</sub> is independently selected from H, C<sub>1-4</sub> alkyl,  
10 C<sub>3-4</sub> alkenyl, C<sub>3-4</sub> alkynyl, C<sub>3-6</sub> cycloalkyl, and phenyl; each of NR<sub>C</sub>R<sub>D</sub>, NR<sub>E</sub>R<sub>F</sub>, and NR<sub>G</sub>R<sub>H</sub> can also be independently morpholinyl, piperazinyl, pyrrolidinyl, or piperadinyl;

- each of R<sub>I</sub> and R<sub>J</sub> is independently H, methyl, or ethyl;  
15 R<sub>K</sub> is C<sub>1-4</sub> alkyl, C<sub>3-4</sub> alkenyl, C<sub>3-4</sub> alkynyl, C<sub>3-6</sub> cycloalkyl, or phenyl;

- X is O, S, or NH; and  
20 wherein each hydrocarbon radical or heterocyclic radical above is optionally substituted with between 1 and 3 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>3-6</sub> cycloalkyl, C<sub>2-4</sub> alkenyl, C<sub>2-4</sub> alkynyl, phenyl, hydroxyl, amino, (amino)sulfonyl, and NO<sub>2</sub>, wherein each substituent alkyl, cycloalkyl, alkenyl, alkynyl or phenyl is in turn optionally substituted with between 1 and 2  
25 substituents independently selected from halo, C<sub>1-2</sub> alkyl, hydroxyl, amino, and NO<sub>2</sub>;

or a pharmaceutically acceptable salt or C<sub>1-7</sub> ester thereof.

28. The method of claim 27, wherein said chronic pain is selected from neuropathic pain, idiopathic pain, and pain associated with chronic alcoholism, vitamin deficiency, uremia, or hypothyroidism.

29. The method of claim 28, wherein said chronic pain is a type of  
5 neuropathic pain.

30. The method of claim 29, wherein said neuropathic pain is associated with one of the following: inflammation, postoperative pain, phantom limb pain, burn pain, gout, trigeminal neuralgia, acute herpetic and postherpetic pain, causalgia, diabetic neuropathy, plexus avulsion, neuroma,  
10 vasculitis, viral infection, crush injury, constriction injury, tissue injury, limb amputation, post-operative pain, arthritis pain, and any other nerve injury between the peripheral nervous system and the central nervous system, inclusively.

15 31. The method of claim 28, wherein said chronic pain is associated with chronic alcoholism, vitamin deficiency, uremia, or hypothyroidism.

32. The method of claim 28, wherein said chronic pain is associated with idiopathic pain.

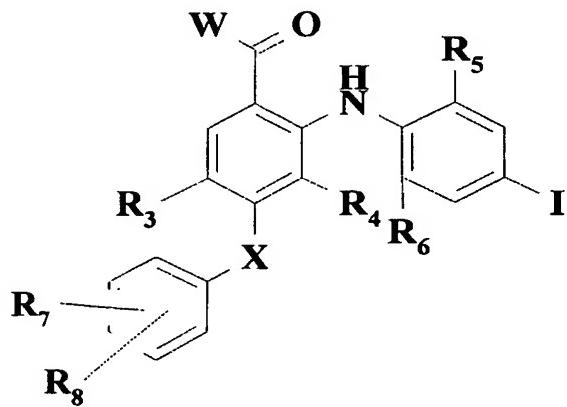
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33. The method of claim 27, wherein said chronic pain is associated with inflammation.

25 34. The method of claim 27, wherein said chronic pain is associated with arthritis.

35. The method of claim 27, wherein said chronic pain is associated with post-operative pain.

36. A method of claim 27, having the following formula (I)A:



(I)A

5 wherein

W is OR<sub>1</sub>, NR<sub>2</sub>OR<sub>1</sub>, NR<sub>A</sub>R<sub>B</sub>, NR<sub>2</sub>NR<sub>A</sub>R<sub>B</sub>, or NR<sub>2</sub>(CH<sub>2</sub>)<sub>2-4</sub>NR<sub>A</sub>R<sub>B</sub>;

R<sub>1</sub> is H, C<sub>1-8</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl, C<sub>3-8</sub> cycloalkyl, phenyl,

10 (phenyl)C<sub>1-4</sub> alkyl, (phenyl)C<sub>3-4</sub> alkenyl, (phenyl)C<sub>3-4</sub> alkynyl, (C<sub>3-8</sub> cycloalkyl)-C<sub>1-4</sub> alkyl, (C<sub>3-8</sub> cycloalkyl)C<sub>3-4</sub> alkenyl, (C<sub>3-8</sub> cycloalkyl)C<sub>3-4</sub> alkynyl, C<sub>3-8</sub> heterocyclic radical, (C<sub>3-8</sub> heterocyclic radical)C<sub>1-4</sub> alkyl, (C<sub>3-8</sub> heterocyclic radical)C<sub>3-4</sub> alkenyl, (C<sub>3-8</sub> heterocyclic radical)C<sub>3-4</sub> alkynyl or (CH<sub>2</sub>)<sub>2-4</sub>NR<sub>A</sub>R<sub>B</sub>;

15

R<sub>2</sub> is H, phenyl, C<sub>1-4</sub> alkyl, C<sub>3-4</sub> alkenyl, C<sub>3-8</sub> alkynyl, C<sub>3-8</sub> cycloalkyl, or (C<sub>3-8</sub> cycloalkyl)-C<sub>1-4</sub> alkyl;

R<sub>A</sub> is H, C<sub>1-6</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl, C<sub>3-8</sub> cycloalkyl, phenyl, (C<sub>3-8</sub> cycloalkyl)C<sub>1-4</sub> alkyl, (C<sub>3-8</sub> cycloalkyl)C<sub>3-4</sub> alkenyl, (C<sub>3-8</sub> cycloalkyl)C<sub>3-4</sub> alkynyl, C<sub>3-8</sub> heterocyclic radical, (C<sub>3-8</sub> heterocyclic radical)C<sub>1-4</sub> alkyl,

20 (aminosulfonyl)phenyl, [(aminosulfonyl)phenyl]C<sub>1-4</sub> alkyl, (aminosulfonyl)C<sub>1-6</sub>

alkyl, (aminosulfonyl)C<sub>3-6</sub>cycloalkyl, or [(aminosulfonyl)C<sub>3-6</sub>cycloalkyl]C<sub>1-4</sub>alkyl;

R<sub>B</sub> is H, C<sub>1-8</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl, C<sub>3-8</sub>cycloalkyl, or C<sub>6-8</sub> aryl;

5

R<sub>3</sub> is halo, NO<sub>2</sub>, SO<sub>2</sub>NR<sub>I</sub>(CH<sub>2</sub>)<sub>2-4</sub>NR<sub>E</sub>R<sub>F</sub>, SO<sub>2</sub>NR<sub>I</sub>R<sub>K</sub> or (CO)T;

T is C<sub>1-8</sub> alkyl, C<sub>3-8</sub>cycloalkyl, (NR<sub>E</sub>R<sub>F</sub>)C<sub>1-4</sub> alkyl, OR<sub>F</sub>, NR<sub>I</sub>(CH<sub>2</sub>)<sub>2-4</sub>NR<sub>E</sub>R<sub>F</sub>, or NR<sub>E</sub>R<sub>F</sub>;

10

R<sub>4</sub> is H or F;

R<sub>5</sub> is H, methyl, halo, or NO<sub>2</sub>;

15 R<sub>6</sub> is H, methyl, halo, or NO<sub>2</sub>;

each of R<sub>7</sub> and R<sub>8</sub> is independently selected from H, halo, C<sub>1-4</sub> alkyl, SO<sub>2</sub>NR<sub>J</sub>(CH<sub>2</sub>)<sub>2-4</sub>NR<sub>G</sub>R<sub>H</sub>, (CO)(CH<sub>2</sub>)<sub>2-4</sub>NR<sub>G</sub>R<sub>H</sub>, (CO)NR<sub>J</sub>(CH<sub>2</sub>)<sub>2-4</sub>NR<sub>G</sub>R<sub>H</sub>, (CO)O(CH<sub>2</sub>)<sub>2-4</sub>NR<sub>G</sub>R<sub>H</sub>, SO<sub>2</sub>NR<sub>G</sub>R<sub>H</sub>, and (CO)NR<sub>G</sub>R<sub>H</sub>;

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each of R<sub>C</sub>, R<sub>D</sub>, R<sub>E</sub>, R<sub>F</sub>, R<sub>G</sub>, and R<sub>H</sub> is independently selected from H, C<sub>1-4</sub> alkyl,

C<sub>3-4</sub> alkenyl, C<sub>3-4</sub> alkynyl, C<sub>3-6</sub>cycloalkyl, and phenyl; each of NR<sub>C</sub>R<sub>D</sub>, NR<sub>E</sub>R<sub>F</sub>, and NR<sub>G</sub>R<sub>H</sub> can also be independently morpholinyl, piperazinyl, pyrrolidinyl, or piperadinyll;

25

each of R<sub>I</sub> and R<sub>J</sub> is independently H, methyl, or ethyl;

R<sub>K</sub> is C<sub>1-4</sub> alkyl, C<sub>3-4</sub> alkenyl, C<sub>3-4</sub> alkynyl, C<sub>3-6</sub>cycloalkyl, or phenyl;

30

X is O, S, or NH; and

wherein each hydrocarbon radical or heterocyclic radical above is optionally substituted with between 1 and 3 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>3-6</sub> cycloalkyl, C<sub>2-4</sub> alkenyl, C<sub>2-4</sub> alkynyl, phenyl, hydroxyl, amino, (amino)sulfonyl, and NO<sub>2</sub>, wherein each substituent alkyl, cycloalkyl,

- 5 alkenyl, alkynyl or phenyl is in turn optionally substituted with between 1 and 2 substituents independently selected from halo, C<sub>1-2</sub> alkyl, hydroxyl, amino, and NO<sub>2</sub>;

or a pharmaceutically acceptable salt or C<sub>1-7</sub> ester thereof.

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37. A method of claim 27, wherein R<sub>3</sub> is NO<sub>2</sub>.

38. A method of claim 27, wherein R<sub>4</sub> is fluoro.

15

39. A method of claim 27, wherein each of R<sub>3</sub> and R<sub>4</sub> is independently selected from H and fluoro.

40. A method of claim 27, wherein R<sub>5</sub> is methyl, fluoro, or chloro.

20

41. A method of claim 27, wherein R<sub>6</sub> is methyl, chloro, fluoro, nitro, or hydrogen.

42. A method of claim 41, wherein R<sub>6</sub> is H.

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43. A method of claim 41, wherein R<sub>6</sub> is fluoro.

44. A method of claim 27, wherein R<sub>K</sub> is methyl or ethyl.

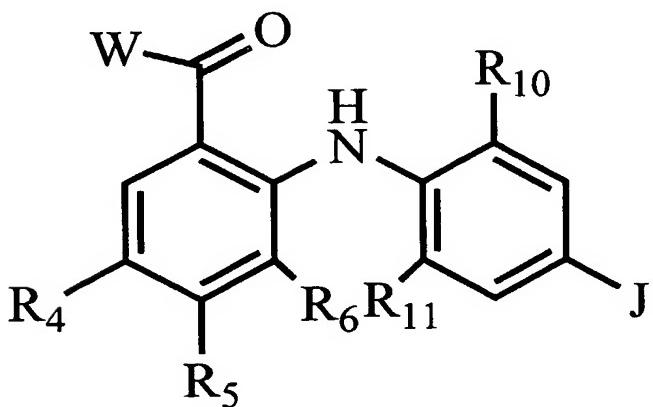
45. A method of claim 27, wherein R<sub>1</sub> is H, methyl, ethyl, propyl, 30 isopropyl, isobutyl, benzyl, phenyl, phenethyl, allyl, C<sub>2-5</sub> alkenyl, C<sub>3-6</sub> cycloalkyl, (C<sub>3-5</sub> cycloalkyl)C<sub>1-2</sub> alkyl, (C<sub>3-5</sub> heterocyclic radical)C<sub>1-2</sub> alkyl, or (CH<sub>2</sub>)<sub>2-4</sub> NR<sub>C</sub>R<sub>D</sub>.

46. A method of claim 45, wherein R<sub>1</sub> is H or (C<sub>3-4</sub> cycloalkyl)-C<sub>1-2</sub> alkyl.
- 5 47. A method of claim 27, wherein R<sub>2</sub> is H or methyl.
48. A method of claim 27, wherein R<sub>A</sub> has at least one hydroxyl substituent.
- 10 49. A method of claim 27, wherein R<sub>A</sub> is H, methyl, ethyl, isobutyl, hydroxyethyl, phenyl, 2-piperidin-1-yl-ethyl, 2,3-dihydroxy-propyl, 3-[4-(2-hydroxyethyl)-piperazin-1-yl]-propyl, 2-pyrrolidin-1-yl-ethyl, or 2-diethylaminoethyl; and R<sub>B</sub> is H; or where R<sub>B</sub> is methyl and R<sub>A</sub> is phenyl.
- 15 50. A method of claim 27, wherein W is NR<sub>A</sub>R<sub>B</sub> or NR<sub>2</sub>NR<sub>A</sub>R<sub>B</sub>.
51. A method of claim 27, wherein W is NR<sub>2</sub>(CH<sub>2</sub>)<sub>2-4</sub>NR<sub>A</sub>R<sub>B</sub> or O(CH<sub>2</sub>)<sub>2-3</sub>NR<sub>A</sub>R<sub>B</sub>.
- 20 52. A method of claim 27, wherein W is NR<sub>2</sub>OR<sub>1</sub>.
53. A method of claim 27, wherein W is OR<sub>B</sub>.
54. A method of claim 27, wherein R<sub>7</sub> is in the para position relative  
25 to X.
55. A method of claim 54, wherein R<sub>7</sub> is iodo.
56. A method of claim 27, wherein R<sub>8</sub> is in the ortho position relative  
30 to X.

57. A method of claim 27 having the formula 2,4-bis-(2-chloro-4-iodo-phenylamino)-3-fluoro-5-nitro-benzoic acid.

58. A method of claim 27, wherein said MEK inhibitor has a  
 5 structure selected from: 2-(2-chloro-4-iodo-phenylamino)-3-fluoro-5-nitro-4-(4-sulfamoyl-phenylamino)-benzoic acid; 2-(2-chloro-4-iodo-phenylamino)-3-fluoro-5-nitro-4-phenylamino-benzoic acid; 2-(2-chloro-4-iodo-phenylamino)-3-fluoro-5-nitro-4-phenoxy-benzoic acid; 2-(2-chloro-4-iodo-phenylamino)-3-fluoro-5-nitro-4-phenylsulfanyl-benzoic acid; 2-(2-chloro-4-iodo-phenylamino)-3-fluoro-4-(methyl-phenyl-amino)-5-nitro-benzoic acid; benzamide, 2-[(2-chloro-4-iodophenyl)amino]-3-fluoro-N-hydroxy-4-[[4-[(2-hydroxyethyl)amino]-carbonyl]phenyl]amino]-5-nitro-; benzamide, 2-[(2-chloro-4-iodophenyl)amino]-4-[[4-[(dimethylamino)carbonyl]phenyl]amino]-3-fluoro-N-hydroxy-5-nitro-; 2-(2-chloro-4-iodo-phenylamino)-3,5-difluoro-4-phenylamino-benzoic acid; 2-(2-chloro-4-iodo-phenylamino)-3-fluoro-5-nitro-4-(3-sulfamoyl-phenylamino)-benzoic acid; and 2-(2-chloro-4-iodo-phenylamino)-3-fluoro-5-nitro-4-(2-sulfamoyl-phenylamino)-benzoic acid; and the corresponding hydroxamic acids and cyclopropylmethyl hydroxamates.

59. A method for treating chronic pain, said method comprising administering to a subject in need of such treatment a composition comprising a MEK inhibitor selected from a compound of formula (I)B:



wherein

- 5 W is OR<sub>1</sub>, NR<sub>2</sub>OR<sub>1</sub>, NR<sub>A</sub>R<sub>B</sub>, NR<sub>2</sub>NR<sub>A</sub>R<sub>B</sub>, O(CH<sub>2</sub>)<sub>1-4</sub>NR<sub>A</sub>R<sub>B</sub>, or NR<sub>2</sub>(CH<sub>2</sub>)<sub>1-4</sub>NR<sub>A</sub>R<sub>B</sub>;  
O(CH<sub>2</sub>)<sub>1-4</sub>OR<sub>1</sub>, or NR<sub>2</sub>(CH<sub>2</sub>)<sub>1-4</sub>OR<sub>1</sub>;

- 10 R<sub>1</sub> is H, C<sub>1-8</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl, C<sub>3-8</sub> cycloalkyl, phenyl, (phenyl)C<sub>1-4</sub> alkyl, (phenyl)C<sub>3-4</sub> alkenyl, (phenyl)C<sub>3-4</sub> alkynyl, (C<sub>3-8</sub> cycloalkyl)-C<sub>1-4</sub> alkyl, (C<sub>3-8</sub> cycloalkyl)C<sub>3-4</sub> alkenyl, (C<sub>3-8</sub> cycloalkyl)C<sub>3-4</sub> alkynyl, C<sub>3-8</sub> heterocyclic radical, (C<sub>3-8</sub> heterocyclic radical)C<sub>1-4</sub> alkyl, (C<sub>3-8</sub> heterocyclic radical)C<sub>3-4</sub> alkenyl, or (C<sub>3-8</sub> heterocyclic radical)C<sub>3-4</sub> alkynyl;

- 15 each of R<sub>2</sub> and R<sub>3</sub> is independently H, phenyl, C<sub>1-4</sub> alkyl, C<sub>3-8</sub> alkynyl, C<sub>3-8</sub> cycloalkyl, or (C<sub>3-8</sub> cycloalkyl)C<sub>1-4</sub> alkyl;

each of R<sub>4</sub>, R<sub>5</sub> and R<sub>6</sub> is independently H, Cl, F, or Br;

- 20 R<sub>A</sub> is H, C<sub>1-6</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl, C<sub>3-8</sub> cycloalkyl, phenyl, (C<sub>3-8</sub> cycloalkyl)C<sub>1-4</sub> alkyl, (C<sub>3-8</sub> cycloalkyl)C<sub>3-4</sub> alkenyl, (C<sub>3-8</sub> cycloalkyl)C<sub>3-4</sub> alkynyl, C<sub>3-8</sub> heterocyclic radical, (C<sub>3-8</sub> heterocyclic radical)C<sub>1-4</sub> alkyl, (aminosulfonyl)phenyl, [(aminosulfonyl)phenyl]C<sub>1-4</sub> alkyl, (aminosulfonyl)C<sub>1-6</sub> alkyl, (aminosulfonyl)C<sub>3-6</sub> cycloalkyl, or [(aminosulfonyl)C<sub>3-6</sub> cycloalkyl]C<sub>1-4</sub> alkyl;

R<sub>B</sub> is H, C<sub>1-8</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl, C<sub>3-8</sub> cycloalkyl, or phenyl;

- 30 J is SR<sub>C</sub>, OR<sub>C</sub>, SO<sub>2</sub>R<sub>C</sub>, SOR<sub>C</sub>, SO<sub>2</sub>NR<sub>D</sub>R<sub>E</sub>, C<sub>1-8</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl, C<sub>3-8</sub> cycloalkyl, C<sub>5-8</sub> cycloalkenyl, phenyl, (C<sub>3-8</sub> cycloalkyl)C<sub>1-4</sub> alkyl,

(C<sub>3-8</sub> cycloalkyl)C<sub>3-4</sub> alkenyl, (C<sub>3-8</sub> cycloalkyl)C<sub>3-4</sub> alkynyl, C<sub>3-8</sub> heterocyclic radical, (C<sub>3-8</sub> heterocyclic radical)C<sub>1-4</sub> alkyl, -M'E'G', (heterocyclic radical)-M'-E'-G', or (cycloalkyl)-M'-E'-G';

5 M' is O, SO, SO<sub>2</sub>, NR<sub>E</sub>, (CO)NR<sub>E</sub>, NR<sub>E</sub>(CO), SO<sub>2</sub>NR<sub>E</sub>, NR<sub>E</sub>SO<sub>2</sub>, or CH<sub>2</sub>;

E' is absent (a covalent bond), (CH<sub>2</sub>)<sub>1-4</sub> or (CH<sub>2</sub>)<sub>m</sub>O(CH<sub>2</sub>)<sub>p</sub> where 1 ≤ (each of m and p independently) ≤ 3 and 2 ≤ (m + p) ≤ 4;

10 G' is OR<sub>3</sub>, SO<sub>2</sub>R<sub>C</sub>, or NR<sub>F</sub>R<sub>G</sub>; provided that where p = 1, then G' is H; each of R<sub>C</sub>, R<sub>D</sub>, R<sub>E</sub>, R<sub>F</sub> and R<sub>G</sub> is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>3-4</sub> alkenyl, C<sub>3-4</sub> alkynyl, C<sub>3-6</sub> cycloalkyl, C<sub>3-6</sub> heterocyclic radical, 15 and phenyl; NR<sub>F</sub>R<sub>G</sub> and NR<sub>D</sub>R<sub>E</sub> can each also independently be selected from morpholinyl, pyrazinyl, piperazinyl, pyrrolidinyl, or piperadinyl;

R<sub>10</sub> is H, C<sub>1-4</sub> alkyl, halo, NO<sub>2</sub>, or SO<sub>2</sub>NR<sub>H</sub>R<sub>I</sub>; and  
20 R<sub>11</sub> is H, halo, or NO<sub>2</sub>;

wherein each hydrocarbon radical or heterocyclic radical above is optionally substituted with between 1 and 3 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>3-6</sub> cycloalkyl, C<sub>2-4</sub> alkenyl, C<sub>2-4</sub> alkynyl, phenyl, hydroxy, 25 amino, (amino)sulfonyl, and NO<sub>2</sub>, wherein each substituent alkyl, cycloalkyl, alkenyl, alkynyl or phenyl is in turn optionally substituted with between 1 and 3 substituents independently selected from halo, C<sub>1-2</sub> alkyl, hydroxy, amino, and NO<sub>2</sub>;  
30 or a pharmaceutically acceptable salt or C<sub>1-7</sub> ester thereof.

60. The method of claim 59, wherein said chronic pain is selected from neuropathic pain, idiopathic pain, and pain associated with chronic alcoholism, vitamin deficiency, uremia, or hypothyroidism.

61. The method of claim 60, wherein said chronic pain is a type of  
5 neuropathic pain.

62. The method of claim 61, wherein said neuropathic pain is associated with one of the following: inflammation, postoperative pain, phantom limb pain, burn pain, gout, trigeminal neuralgia, acute herpetic and postherpetic pain, causalgia, diabetic neuropathy, plexus avulsion, neuroma,  
10 vasculitis, viral infection, crush injury, constriction injury, tissue injury, limb amputation, post-operative pain, arthritis pain, and any other nerve injury between the peripheral nervous system and the central nervous system, inclusively.

15 63. The method of claim 60, wherein said chronic pain is associated with chronic alcoholism, vitamin deficiency, uremia, or hypothyroidism.

64. The method of claim 60, wherein said chronic pain is associated with idiopathic pain.

20 65. The method of claim 59, wherein said chronic pain is associated with inflammation.

66. The method of claim 59, wherein said chronic pain is associated  
25 with arthritis.

67. The method of claim 59, wherein said chronic pain is associated with post-operative pain.

30 68. A method of claim 59, wherein R<sub>c</sub> is C<sub>1-2</sub> alkyl.

69. A method of claim 59, wherein W is OH.
70. A method of claim 59, wherein W is NHOH.
- 5 71. A method of claim 59, wherein W is NHO(cyclopropylmethyl).
72. A method of claim 59, wherein R<sub>10</sub> is methyl or chloro.
- 10 73. A method of claim 59, where R<sub>11</sub> is fluoro.
74. A method of claim 59, where R<sub>11</sub> is H.
75. A method of claim 59, wherein J is trihalomethyl or methylthio.
- 15 76. A method of claim 59, wherein J is 1,2,5-thiadiazol-3-yl.
77. A method of claim 59, wherein J is SO<sub>2</sub>CH<sub>3</sub>.
- 20 78. A method of claim 59, wherein J is SOCH<sub>3</sub>.
79. A method of claim 59, wherein J is C<sub>2-8</sub> alkynyl where the triple bond is between the carbon atoms alpha and beta to the phenyl group.
- 25 80. A method of claim 59, wherein R<sub>1</sub> has at least one hydroxy substituent.
81. A method of claim 59, wherein R<sub>1</sub> is H, methyl, ethyl, propyl, isopropyl, isobutyl, benzyl, phenethyl, allyl, C<sub>3-5</sub> alkenyl, C<sub>3-5</sub> alkynyl, 30 C<sub>3-6</sub> cycloalkyl, (C<sub>3-5</sub> cycloalkyl)C<sub>1-2</sub> alkyl, or (C<sub>3-5</sub> heterocyclic radical)-C<sub>1-2</sub> alkyl.

82. A method of claim 59, wherein R<sub>1</sub> is H or (C<sub>3-4</sub> cycloalkyl)-C<sub>1-2</sub> alkyl.

83. A method of claim 59, wherein R<sub>2</sub> is H, methyl, C<sub>3-4</sub> alkynyl, C<sub>3-5</sub> cycloalkyl, or (C<sub>3-5</sub> cycloalkyl)methyl.

84. A method of claim 59, wherein R<sub>A</sub> is H, methyl, ethyl, isobutyl, hydroxyethyl, hydroxypropyl, cyclopropylmethyl, cyclobutylmethyl, C<sub>2-4</sub> alkynyl, phenyl, 2-piperidin-1-yl-ethyl, 2,3-dihydroxy-propyl, 3-[4-(2-hydroxyethyl)-piperazin-1-yl]-propyl, 2-pyrrolidin-1-yl-ethyl, or 2-diethylaminoethyl; and R<sub>B</sub> is H; or where R<sub>B</sub> is methyl and R<sub>A</sub> is phenyl.

85. A method of claim 59, wherein each of R<sub>4</sub> and R<sub>6</sub> is H, and R<sub>5</sub> is F.

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86. A method of claim 59, wherein each of R<sub>4</sub>, R<sub>5</sub>, and R<sub>6</sub> is F.

87. A method of claim 59, wherein each of R<sub>4</sub> and R<sub>5</sub> is F and R<sub>6</sub> is Br.

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88. A method of claim 59, wherein R<sub>5</sub> is F.

89. A method of claim 59, wherein said MEK inhibitor has a structure selected from: 4-fluoro-2-(2-methyl-4-methylsulfanyl-phenylamino)-benzoic acid; 5-bromo-3,4-difluoro-2-(2-methyl-4-methylsulfanyl-phenylamino)-benzoic acid; 3,4-difluoro-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzoic acid; 2-(4-methanesulfinyl-2-methyl-phenylamino)-benzoic acid; 3,4,5-trifluoro-2-(4-methanesulfonyl-2-methyl-phenylamino)-benzoic acid; 3,4-difluoro-2-(2-methyl-4-methylsulfanyl-phenylamino)-benzoic acid; 2-(2-methyl-4-methylsulfanyl-phenylamino)-4-nitro-benzoic acid;

- 3,4,5-trifluoro-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzoic acid; 4-fluoro-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzoic acid; 5-bromo-3,4-difluoro-2-(4-methanesulfonyl-2-methyl-phenylamino)-benzoic acid; 3,4,5-trifluoro-2-(2-methyl-4-methylsulfanyl-phenylamino)-benzoic acid; 4-fluoro-2-(4-methane-sulfinyl-2-methyl-phenylamino)-benzoic acid; 5-bromo-3,4-difluoro-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzoic acid; 3,4-difluoro-2-(4-methanesulfonyl-2-methyl-phenylamino)-benzoic acid; 2-(4-methanesulfonyl-2-methyl-phenylamino)-4-nitro-benzoic acid; N-cyclopropylmethoxy-4-fluoro-2-(2-methyl-4-methylsulfanyl-phenylamino)-benzamide; 5-bromo-N-cyclopropylmethoxy-3,4-difluoro-2-(2-methyl-4-methylsulfanyl-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-2-(4-methanesulfinyl-2-methyl-phenylamino)-4-nitro-benzamide; N-cyclopropylmethoxy-3,4,5-trifluoro-2-(4-methanesulfonyl-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(2-methyl-4-methylsulfanyl-phenylamino)-benzamide; N-cyclopropylmethoxy-2-(2-methyl-4-methylsulfanyl-phenylamino)-4-nitro-benzamide; N-cyclopropylmethoxy-3,4,5-trifluoro-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-4-fluoro-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzamide; 5-bromo-N-cyclopropylmethoxy-3,4-difluoro-2-(4-methanesulfonyl-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4,5-trifluoro-2-(2-methyl-4-methylsulfanyl-phenylamino)-benzamide; N-cyclopropylmethoxy-4-fluoro-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzamide; 5-bromo-N-cyclopropylmethoxy-3,4-difluoro-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-methanesulfonyl-2-methyl-phenylamino)-benzamide; and N-cyclopropylmethoxy-2-(4-methanesulfonyl-2-methyl-phenylamino)-4-nitro-benzamide.
- 30 90. A method of claim 59, wherein said MEK inhibitor has a structure selected from: 4-fluoro-N-hydroxy-2-(2-methyl-4-methylsulfanyl-phenylamino)-benzamide; 5-bromo-3,4-difluoro-N-hydroxy-2-(2-methyl-4-

methylsulfanyl-phenylamino)-benzamide; 3,4-difluoro-N-hydroxy-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzamide; N-hydroxy-2-(4-methanesulfinyl-2-methyl-phenylamino)-4-nitro-benzamide; 3,4,5-trifluoro-N-hydroxy-2-(4-methanesulfonyl-2-methyl-phenylamino)-benzamide; 3,4-difluoro-N-hydroxy-2-(2-methyl-4-methylsulfanyl-phenylamino)-benzamide; N-hydroxy-2-(2-methyl-4-methylsulfanyl-phenylamino)-4-nitro-benzamide; 8:3,4,5-trifluoro-N-hydroxy-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzamide; 4-fluoro-N-hydroxy-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzamide; 5-bromo-3,4-difluoro-N-hydroxy-2-(4-methanesulfonyl-2-methyl-phenylamino)-benzamide; 3,4,5-trifluoro-N-hydroxy-2-(2-methyl-4-methylsulfanyl-phenylamino)-benzamide; 4-fluoro-N-hydroxy-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzamide; 5-bromo-3,4-difluoro-N-hydroxy-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzamide; 3,4-difluoro-N-hydroxy-2-(4-methanesulfonyl-2-methyl-phenylamino)-benzamide; and N-hydroxy-2-(4-methanesulfonyl-2-methyl-phenylamino)-4-nitro-benzamide.

91. A method of claim 59, wherein said MEK inhibitor has a structure selected from: 3,4-difluoro-2-(4-imidazol-1-yl-2-methyl-phenylamino)-benzoic acid; N-cyclopropylmethoxy-3,4-difluoro-2-(4-imidazol-1-yl-2-methyl-phenylamino)-benzamide; 3,4-difluoro-N-hydroxy-2-(4-imidazol-1-yl-2-methyl-phenylamino)-benzamide; 3,4,5-trifluoro-2-(2-methyl-4-[1,2,5]thiadiazol-3-yl-phenylamino)-benzoic acid; N-cyclopropylmethoxy-3,4,5-trifluoro-2-(2-methyl-4-[1,2,5]thiadiazol-3-yl-phenylamino)-benzamide; 3,4,5-trifluoro-N-hydroxy-2-(2-methyl-4-[1,2,5]thiadiazol-3-yl-phenylamino)-benzamide; 2-[4-(4-chloro-[1,2,5]thiadiazol-3-yl)-2-methyl-phenylamino]-3,4,5-trifluoro-benzoic acid; 2-[4-(4-chloro-[1,2,5]thiadiazol-3-yl)-2-methyl-phenylamino]-N-cyclopropylmethoxy-3,4,5-trifluoro-benzamide; 2-[4-(4-chloro-[1,2,5]thiadiazol-3-yl)-2-methyl-phenylamino]-3,4,5-trifluoro-N-hydroxy-benzamide; 2-{4-[4-(2-dimethylamino-ethoxy)-[1,2,5]thiadiazol-3-yl]-2-methyl-phenylamino}-3,4,5-trifluoro-benzoic acid; N-cyclopropylmethoxy-3,4,5-trifluoro-2-{2-methyl-4-[4-(2-piperidin-1-yl-ethoxy)-[1,2,5]thiadiazol-3-yl]}

phenylamino}-benzamide; and 3,4,5-trifluoro-N-hydroxy-2-{2-methyl-4-[4-(2-morpholin-4-yl-ethoxy)-[1,2,5]thiadiazol-3-yl]-phenylamino}-benzamide.

92. The method of claim 59, wherein said MEK inhibitor has a  
5 structure selected from: 5-bromo-2-(2-chloro-4-methylsulfanyl-phenylamino)-3,4-difluoro-benzoic acid; 2-(2-chloro-4-methanesulfinyl-phenylamino)-3,4-difluoro-benzoic acid; 2-(2-chloro-4-methanesulfonyl-phenylamino)-3,4,5-trifluoro-benzoic acid; 2-(2-chloro-methylsulfanyl-phenylamino)-3,4-difluoro-benzoic acid; 5-bromo-2-(2-chloro-4-methanesulfonyl-phenylamino)-3,4-difluoro-benzoic acid; 2-(2-Chloro-4-methanesulfonyl-phenylamino)-3,4-difluoro-benzoic acid; 5-bromo-2-(2-chloro-4-methylsulfanyl-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-benzamide; 2-(2-chloro-4-methanesulfinyl-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-benzamide; 2-(2-chloro-4-methanesulfonyl-phenylamino)- N-cyclopropylmethoxy-3,4,5-trifluoro-benzamide; 2-(2-chloro-4-methylsulfanyl-phenylamino)- N-cyclopropylmethoxy-3,4-difluoro-benzamide;  
10 2-(2-chloro-4-methanesulfinyl-phenylamino)- N-cyclopropylmethoxy-3,4,5-trifluoro-benzamide; 5-bromo-2-(2-chloro-4-methanesulfonyl-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-benzamide; 2-(2-chloro-4-methanesulfonyl-phenylamino)- N-cyclopropylmethoxy-3,4,5-trifluoro-benzamide; 2-(2-chloro-4-methylsulfanyl-phenylamino)- N-cyclopropylmethoxy-3,4-difluoro-benzamide;  
15 2-(2-chloro-4-methanesulfinyl-phenylamino)- N-cyclopropylmethoxy-3,4,5-trifluoro-benzamide; 5-bromo-2-(2-chloro-4-methanesulfonyl-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-benzamide; 2-(2-chloro-4-methanesulfonyl-phenylamino)- N-cyclopropylmethoxy-3,4,5-trifluoro-benzamide; 2-(2-chloro-4-methylsulfanyl-phenylamino)- N-cyclopropylmethoxy-3,4-difluoro-benzamide;  
20 2-(2-chloro-4-methanesulfinyl-phenylamino)- N-cyclopropylmethoxy-3,4,5-trifluoro-benzamide; 2-(2-chloro-4-methanesulfonyl-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-benzamide; 2-[2-chloro 4-(3H-imidazol-1-yl)-phenylamino]-N-cyclopropylmethoxy-3,4-difluoro-benzamide; 2-(2-chloro-4-[1,2,5]thiadiazol-3-yl-phenylamino)-N-cyclopropylmethoxy-3,4,5-trifluoro-benzamide; 2-[4-(2-chloro-4-chloro-  
25 [1,2,5]thiadiazol-3-yl)-phenylamino]-3,4,5-trifluoro-benzoic acid; 2-[2-chloro-4-(4-chloro-[1,2,5]thiadiazol-3-yl)-phenylamino]-N-cyclopropylmethoxy-3,4,5-trifluoro-benzamide; 2-{4-[4-(2-dimethylamino-ethoxy)-[1,2,5]thiadiazol-3-yl]-2-methyl-phenylamino}-3,4,5-trifluoro-benzoic acid; and 2-{2-chloro-4-[4-(2-piperidin-1-yl-ethoxy)-[1,2,5]thiadiazol-3-yl]-phenylamino}-N-  
30 cyclopropylmethoxy-3,4,5-trifluoro-benzamide.

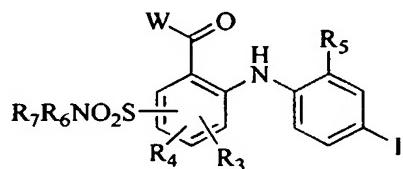
93. The method of claim 59, wherein said MEK inhibitor has a structure selected from: 2-(4-Ethynyl-2-methyl-phenylamino)-4-fluoro-benzoic acid; 5-Bromo-2-(4-ethynyl-2-methyl-phenylamino)-3,4-difluoro-benzoic acid; N-Cyclopropylmethoxy-2-(4-ethynyl-2-methyl-phenylamino)-3,4-difluoro-  
5 benzamide; N-Cyclopropylmethoxy-2-(4-ethynyl-2-methyl-phenylamino)-4-nitro-Benzamide; 2-(4-Ethynyl-2-methyl-phenylamino)-3,4,5-trifluoro-N-hydroxy-benzamide; 2-(4-Ethynyl-2-methyl-phenylamino)-3,4-difluoro-benzoic acid; 2-(4-Ethynyl-2-methyl-phenylamino)-4-nitro-benzoic acid; N-Cyclopropylmethoxy-2-(4-ethynyl-2-methyl-phenylamino)-3,4,5-trifluoro-  
10 benzamide; 4-Fluoro-N-hydroxy-2-(4-methanesulfinyl-2-methyl-phenylamino)-benzamide; 5-Bromo-2-(4-ethynyl-2-methyl-phenylamino)-3,4-difluoro-N-hydroxy-benzamide; 2-(4-Ethynyl-2-methyl-phenylamino)-3,4,5-trifluoro-benzoic acid; N-Cyclopropylmethoxy-2-(4-ethynyl-2-methyl-phenylamino)-4-fluoro-benzamide; 5-Bromo-N-cyclopropylmethoxy-2-(4-ethynyl-2-methyl-  
15 phenylamino)-3,4-difluoro-benzamide; 2-(4-Ethynyl-2-methyl-phenylamino)-3,4-difluoro-N-hydroxy-benzamide; 2-(4-Ethynyl-2-methyl-phenylamino)-N-hydroxy-4-nitro-benzamide; 2-(4-Ethynyl-2-methyl-phenylamino)-4-fluoro-benzoic acid; N-Cyclopropylmethoxy-2-(4-ethynyl-2-methyl-phenylamino)-4-fluoro-benzamide; and 4-Fluoro-N-hydroxy-2-(4-methanesulfinyl-2-methyl-  
20 phenylamino)-benzamide.

94. The method of claim 59, wherein said MEK inhibitor has a structure selected from: 2-(2-Chloro-4-ethynyl-phenylamino)-4-fluoro-benzoic acid; 5-Bromo-2-(2-chloro-4-ethynyl-phenylamino)-3,4-difluoro-benzoic acid; 2-(2-Chloro-4-ethynyl-phenylamino)- N-cyclopropylmethoxy-3,4-difluoro-benzamide; 2-(2-Chloro-4-ethynyl-phenylamino)- N-cyclopropylmethoxy-4-nitro-benzamide; 2-(2-Chloro-4-ethynyl-phenylamino)- N-hydroxy-3,4,5-trifluoro- benzamide; 2-(2-Chloro-4-ethynyl-phenylamino)-3,4-difluoro-benzoic acid; 2-(4-Ethynyl-2-chloro-phenylamino)-4-nitro-benzoic acid; 2-(2-Chloro-4-ethynyl-phenylamino)- N-Cyclopropylmethoxy-3,4,5-trifluoro-benzamide; 2-(2-chloro-4-methanesulfinyl-phenylamino)- 4-fluoro-N-hydroxy-benzamide; 5-Bromo-2-(4-ethynyl-2-chloro-phenylamino)-3,4-difluoro-N-hydroxy-benzamide; 2-(2-Chloro-4-ethynyl-phenylamino)-3,4,5-trifluoro-benzoic acid; 2-(2-Chloro-

4-ethynyl-phenylamino)- N-cyclopropylmethoxy-4-fluoro-benzamide; 5-Bromo-  
 2-(2-chloro-4-ethynyl-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-  
 benzamide; 2-(4-Ethynyl-2-chloro-phenylamino)-3,4-difluoro-N-hydroxy-  
 benzamide; 2-(4-Ethynyl-2-chloro-phenylamino)-N-hydroxy-4-nitro-  
 5 benzamide; 2-(2-Chloro-4-ethynyl-phenylamino)-4-fluoro-benzoic acid; 2-(2-  
 Chloro-4-ethynyl-phenylamino)- N-cyclopropylmethoxy-4-fluoro-benzamide; 2-  
 (2-Chloro-4-methanesulfinyl-phenylamino)- 4-fluoro-N-hydroxy-benzamide;  
 and 2-(2-chloro-4-imidazol-1-yl-phenylamino)- 3,4-Difluoro-benzoic acid.

10 95. A method for treating chronic pain, said method comprising  
 administering to a subject in need of such treatment a composition comprising  
 a MEK inhibitor selected from a compound of formula (I)C:

15



(I)C

20

25 wherein

W is OR<sub>1</sub>, NR<sub>2</sub>OR<sub>1</sub>, NR<sub>A</sub>R<sub>B</sub>, NR<sub>2</sub>NR<sub>A</sub>R<sub>B</sub>, or NR<sub>2</sub>(CH<sub>2</sub>)<sub>2-4</sub>NR<sub>A</sub>R<sub>B</sub>;

30 R<sub>1</sub> is H, C<sub>1-8</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl, C<sub>3-8</sub> cycloalkyl, phenyl,  
 (phenyl)C<sub>1-4</sub> alkyl, (phenyl)C<sub>3-4</sub> alkenyl, (phenyl)C<sub>3-4</sub> alkynyl, (C<sub>3-8</sub>  
 cycloalkyl)-

C<sub>1-4</sub> alkyl, (C<sub>3-8</sub> cycloalkyl)C<sub>3-4</sub> alkenyl, (C<sub>3-8</sub> cycloalkyl)C<sub>3-4</sub> alkynyl, C<sub>3-8</sub> heterocyclic radical, (C<sub>3-8</sub> heterocyclic radical)C<sub>1-4</sub> alkyl, (C<sub>3-8</sub> heterocyclic radical)C<sub>3-4</sub> alkenyl, (C<sub>3-8</sub> heterocyclic radical)C<sub>3-4</sub> alkynyl or (CH<sub>2</sub>)<sub>2-4</sub>NR<sub>A</sub>R<sub>B</sub>;

5 R<sub>2</sub> is H, phenyl, C<sub>1-4</sub> alkyl, C<sub>3-4</sub> alkenyl, C<sub>3-8</sub> alkynyl, C<sub>3-8</sub> cycloalkyl, or (C<sub>3-8</sub> cycloalkyl)-C<sub>1-4</sub> alkyl;

10 R<sub>A</sub> is H, C<sub>1-6</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl, C<sub>3-8</sub> cycloalkyl, phenyl, (C<sub>3-8</sub> cycloalkyl)C<sub>1-4</sub> alkyl, (C<sub>3-8</sub> cycloalkyl)C<sub>3-4</sub> alkenyl, (C<sub>3-8</sub> cycloalkyl)C<sub>3-4</sub> alkynyl, C<sub>3-8</sub> heterocyclic radical, (C<sub>3-8</sub> heterocyclic radical)C<sub>1-4</sub> alkyl, (aminosulfonyl)phenyl, [(aminosulfonyl)phenyl]C<sub>1-4</sub> alkyl, (aminosulfonyl)C<sub>1-6</sub> alkyl, (aminosulfonyl)C<sub>3-6</sub> cycloalkyl, or [(aminosulfonyl)C<sub>3-6</sub> cycloalkyl]C<sub>1-4</sub> alkyl;

15 R<sub>B</sub> is H, C<sub>1-8</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl, C<sub>3-8</sub> cycloalkyl, or C<sub>6-8</sub> aryl;

R<sub>3</sub> is H, F, Cl, Br, or NO<sub>2</sub>;

R<sub>4</sub> is H or F;

20 R<sub>5</sub> is H, methyl or Cl;

25 R<sub>6</sub> is H, C<sub>1-4</sub> alkyl, hydroxyethyl, hydroxypropyl, (CH<sub>2</sub>)<sub>2-4</sub>(NR<sub>C</sub>R<sub>D</sub>), phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl or CH<sub>2</sub>Ar, where Ar is phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl;

R<sub>7</sub> is H, C<sub>1-4</sub> alkyl, hydroxyethyl, hydroxypropyl, (CH<sub>2</sub>)<sub>2-4</sub>(NR<sub>C</sub>R<sub>D</sub>), phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, or CH<sub>2</sub>Ar, where Ar is phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl;

30 each of R<sub>C</sub> and R<sub>D</sub> is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>3-4</sub> alkenyl,

C<sub>3-4</sub> alkynyl, C<sub>3-6</sub> cycloalkyl, C<sub>3-6</sub> heterocyclic radical, and phenyl; NR<sub>c</sub>R<sub>d</sub> can also be selected from morpholinyl, piperazinyl, pyrrolidinyl, or piperadinyl;

wherein each hydrocarbon radical or heterocyclic radical above is  
5 optionally substituted with between 1 and 3 substituents independently  
selected from halo, C<sub>1-4</sub> alkyl, C<sub>3-6</sub> cycloalkyl, C<sub>2-4</sub> alkenyl, C<sub>2-4</sub> alkynyl,  
phenyl, hydroxy, amino, (amino)sulfonyl, and NO<sub>2</sub>, wherein each substituent  
alkyl, cycloalkyl, alkenyl, alkynyl or phenyl is in turn optionally substituted with  
between 1 and 3 substituents independently selected from halo, C<sub>1-2</sub> alkyl,  
10 hydroxy, amino, and NO<sub>2</sub>;

or a pharmaceutically-acceptable salt or C<sub>1-6</sub> ester thereof.

96. The method of claim 95, wherein said chronic pain is selected  
15 from neuropathic pain, idiopathic pain, and pain associated with chronic  
alcoholism, vitamin deficiency, uremia, or hypothyroidism.

97. The method of claim 96, wherein said chronic pain is a type of  
neuropathic pain.

98. The method of claim 97, wherein said neuropathic pain is  
20 associated with one of the following: inflammation, postoperative pain,  
phantom limb pain, burn pain, gout, trigeminal neuralgia, acute herpetic and  
postherpetic pain, causalgia, diabetic neuropathy, plexus avulsion, neuroma,  
vasculitis, viral infection, crush injury, constriction injury, tissue injury, limb  
amputation, post-operative pain, arthritis pain, and any other nerve injury  
25 between the peripheral nervous system and the central nervous system,  
inclusively.

99. The method of claim 96, wherein said chronic pain is associated  
with chronic alcoholism, vitamin deficiency, uremia, or hypothyroidism.

100. The method of claim 96, wherein said chronic pain is associated with idiopathic pain.

101. The method of claim 95, wherein said chronic pain is associated  
5 with inflammation.

102. The method of claim 95, wherein said chronic pain is associated with arthritis.

10 103. The method of claim 95, wherein said chronic pain is associated with post-operative pain.

104. A method of claim 95, wherein the sulfamoyl group is *meta* to W(CO)- and *para* to the bridging NH..

15 105. A method of claim 95, wherein the sulfamoyl group is *para* to W (CO)- and *meta* to the bridging NH.

106. A method of claim 95, wherein R<sub>4</sub> is fluoro.

20 107. A method of claim 95, where R<sub>3</sub> is fluoro.

108. A method of claim 95, where R<sub>3</sub> is H.

25 109. A method of claim 95, wherein W is OH.

110. A method of claim 95, wherein W is NR<sub>2</sub>OR<sub>1</sub>.

111. A method of claim 109, wherein each of R<sub>3</sub> and R<sub>4</sub> is fluoro.

30 112. A method of claim 95, wherein R<sub>1</sub> has at least one hydroxy substituent.

113. A method of claim 95, wherein R<sub>1</sub> is H, methyl, ethyl, propyl, isopropyl, isobutyl, benzyl, phenethyl, allyl, C<sub>3-5</sub> alkenyl, C<sub>3-5</sub> alkynyl, C<sub>3-6</sub> cycloalkyl, (C<sub>3-5</sub> cycloalkyl)C<sub>1-2</sub> alkyl, or (C<sub>3-5</sub> heterocyclic radical)-5 C<sub>1-2</sub> alkyl.

114. A method of claim 113, wherein R<sub>1</sub> is H or (C<sub>3-4</sub> cycloalkyl)-C<sub>1-2</sub> alkyl.

10 115. A method of claim 95, wherein R<sub>2</sub> is H, methyl, C<sub>3-4</sub> alkynyl, C<sub>3-5</sub> cycloalkyl, or (C<sub>3-5</sub> cycloalkyl)methyl.

15 116. A method of claim 95, wherein R<sub>A</sub> is H, methyl, ethyl, isobutyl, hydroxyethyl, hydroxypropyl, cyclopropylmethyl, cyclobutylmethyl, C<sub>3-4</sub> alkynyl, phenyl, 2-piperidin-1-yl-ethyl, 2,3-dihydroxy-propyl, 3-[4-(2-hydroxyethyl)-piperazin-1-yl]-propyl, 2-pyrrolidin-1-yl-ethyl, or 2-diethylamino-ethyl; and R<sub>B</sub> is H; or where R<sub>B</sub> is methyl and R<sub>A</sub> is phenyl.

20 117. A method of claim 95, wherein R<sub>7</sub> is (CH<sub>2</sub>)<sub>2-4</sub>(NR<sub>C</sub>R<sub>D</sub>).

118. A method of claim 95, wherein NR<sub>C</sub>R<sub>D</sub> is selected from morpholinyl, piperazinyl, pyrrolidinyl, or piperadinyl.

25 119. A method of claim 95, wherein R<sub>5</sub> is methyl or chloro.

120. A method of claim 95, wherein said MEK inhibitor has a structure selected from: 2-(2-chloro-4-iodo-phenylamino)-4-sulfamoyl-benzoic acid; 2-(2-chloro-4-iodo-phenylamino)-N-hydroxy-4-sulfamoyl-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-4-sulfamoyl-benzamide; 30 2-(2-chloro-4-iodo-phenylamino)-4-(2-morpholin-4-yl-ethylsulfamoyl)-benzoic acid; 2-(2-chloro-4-iodo-phenylamino)-N-hydroxy-4-(2-morpholin-4-yl-ethylsulfamoyl)-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-

cyclopropylmethoxy-4-(2-morpholin-4-yl-ethylsulfamoyl)-benzamide; 2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-5-sulfamoyl-benzoic acid; 2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-N-hydroxy-5-sulfamoyl-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-sulfamoyl-benzamide; 2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-5-(2-morpholin-4-yl-ethylsulfamoyl)-benzoic acid; 2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-N-hydroxy-5-(2-morpholin-4-yl-ethylsulfamoyl)-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-(2-morpholin-4-yl-ethylsulfamoyl)-benzamide; 5-(bis-pyridin-3-ylmethyl-sulfamoyl)-3,4-difluoro-2-(4-ido-phenylamino)-benzoic acid; 5-(bis-pyridin-3-ylmethyl-sulfamoyl)-N-cyclopropylmethoxy-3,4-difluoro-2-(4-ido-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-ido-phenylamino)-5-(methyl-pyridin-3-ylmethyl-sulfamoyl)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-ido-phenylamino)-5-[(pyridin-3-ylmethyl)-sulfamoyl]-benzamide; N-  
15 cyclopropylmethoxy-5-[(3-diethylamino-propyl)-pyridin-3-ylmethyl-sulfamoyl]-3,4-difluoro-2-(4-ido-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-5-[(3-hydroxy-propyl)-pyridin-3-ylmethyl-sulfamoyl]-2-(4-ido-phenylamino)-benzamide; N-cyclopropylmethoxy-5-(ethyl-pyridin-3-ylmethyl-sulfamoyl)-3,4-difluoro-2-(4-ido-phenylamino)-benzamide; N-  
20 cyclopropylmethoxy-3,4-difluoro-5-[(2-hydroxy-ethyl)-pyridin-3-ylmethyl-sulfamoyl]-2-(4-ido-phenylamino)-benzamide; 5-(bis-pyridin-2-ylmethyl-sulfamoyl)-3,4-difluoro-2-(4-ido-phenylamino)-benzoic acid; 5-(bis-pyridin-2-ylmethyl-sulfamoyl)-N-cyclopropylmethoxy-3,4-difluoro-2-(4-ido-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-ido-phenylamino)-5-(methyl-pyridin-2-ylmethyl-sulfamoyl)-benzamide; N-  
25 cyclopropylmethoxy-3,4-difluoro-2-(4-ido-phenylamino)-5-[(pyridin-2-ylmethyl)-sulfamoyl]-benzamide; 5-(bis-pyridin-3-ylmethyl-sulfamoyl)-3,4-difluoro-2-(4-ido-2-methyl-phenylamino)-benzoic acid; 5-(bis-pyridin-3-ylmethyl-sulfamoyl)-N-cyclopropylmethoxy-3,4-difluoro-2-(4-ido-2-methyl-phenylamino)-benzamide; N-  
30 cyclopropylmethoxy-3,4-difluoro-2-(4-ido-2-methyl-phenylamino)-5-[(pyridin-



cyclopropylmethoxy-3,4-difluoro-5-[(pyridin-2-ylmethyl)-sulfamoyl]-benzamide; N-cyclopropylmethoxy-3,4-difluoro-5-[(3-hydroxy-propyl)-pyridin-2-ylmethyl-sulfamoyl]-2-(4-iodo-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-5-[(2-hydroxy-ethyl)-pyridin-2-ylmethyl-sulfamoyl]-2-(4-iodo-phenylamino)-benzamide; 5-(benzyl-pyridin-2-ylmethyl-sulfamoyl)-N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-phenylamino)-5-[(pyridin-4-ylmethyl)-sulfamoyl]-benzamide; N-cyclopropylmethoxy-5-(ethyl-pyridin-4-ylmethyl-sulfamoyl)-3,4-difluoro-2-(4-iodo-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-phenylamino)-5-(methyl-pyridin-4-ylmethyl-sulfamoyl)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-5-[(3-hydroxy-propyl)-pyridin-4-ylmethyl-sulfamoyl]-2-(4-iodo-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-5-[(2-hydroxy-ethyl)-pyridin-4-ylmethyl-sulfamoyl]-2-(4-iodo-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-phenylamino)-5-(methyl-phenyl-sulfamoyl)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-phenylamino)-5-phenylsulfamoyl-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-phenylamino)-5-(pyridin-3-ylsulfamoyl)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-5-[(3-hydroxy-propyl)-pyridin-2-ylmethyl-sulfamoyl]-2-(4-iodo-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-5-[(2-hydroxy-ethyl)-pyridin-2-ylmethyl-sulfamoyl]-2-(4-iodo-2-methyl-phenylamino)-benzamide; 5-(benzyl-pyridin-2-ylmethyl-sulfamoyl)-N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-5-(methyl-pyridin-4-ylmethyl-sulfamoyl)-benzamide; N-cyclopropylmethoxy-5-(ethyl-pyridin-4-ylmethyl-sulfamoyl)-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-5-(methyl-pyridin-4-ylmethyl-sulfamoyl)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-5-[(3-hydroxy-propyl)-pyridin-4-ylmethyl-sulfamoyl]-2-(4-iodo-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-5-[(2-hydroxy-ethyl)-pyridin-4-ylmethyl-sulfamoyl]-2-(4-iodo-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-5-[(2-hydroxy-ethyl)-pyridin-4-ylmethyl-sulfamoyl]-2-(4-iodo-2-methyl-phenylamino)-benzamide; N-

cyclopropylmethoxy-3,4-difluoro-2-(4-ido-2-methyl-phenylamino)-5-(methyl-phenyl-sulfamoyl)-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-ido-2-methyl-phenylamino)-5-phenylsulfamoyl-benzamide; N-cyclopropylmethoxy-3,4-difluoro-2-(4-ido-2-methyl-phenylamino)-5-(pyridin-3-ylsulfamoyl)-benzamide; 2-(2-chloro-4-ido-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-[(3-hydroxy-propyl)-pyridin-2-ylmethyl-sulfamoyl]-benzamide; 2-(2-chloro-4-ido-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-[(2-hydroxy-ethyl)-pyridin-2-ylmethyl-sulfamoyl]-benzamide; 5-(benzyl-pyridin-2-ylmethyl-sulfamoyl)-2-(2-chloro-4-ido-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-benzamide; 2-(2-chloro-4-ido-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-[(pyridin-4-ylmethyl)-sulfamoyl]-benzamide; 2-(2-chloro-4-ido-phenylamino)-N-cyclopropylmethoxy-5-(ethyl-pyridin-4-ylmethyl-sulfamoyl)-3,4-difluoro-benzamide; 2-(2-chloro-4-ido-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-(methyl-pyridin-4-ylmethyl-sulfamoyl)-benzamide; 2-(2-chloro-4-ido-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-[(3-hydroxy-propyl)-pyridin-4-ylmethyl-sulfamoyl]-benzamide; 2-(2-chloro-4-ido-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-[(2-hydroxy-ethyl)-pyridin-4-ylmethyl-sulfamoyl]-benzamide; 2-(2-chloro-4-ido-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-(methyl-phenyl-sulfamoyl)-benzamide; 2-(2-chloro-4-ido-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-phenylsulfamoyl-benzamide; 2-(2-chloro-4-ido-phenylamino)-N-cyclopropylmethoxy-3,4-difluoro-5-(pyridin-3-ylsulfamoyl)-benzamide; N-cyclopropylmethoxy-2-(4-ido-phenylamino)-4-phenylsulfamoyl-benzamide; N-cyclopropylmethoxy-2-(4-ido-phenylamino)-4-(pyridin-3-ylsulfamoyl)-benzamide; N-cyclopropylmethoxy-2-(4-ido-phenylamino)-4-[(pyridin-3-ylmethyl)-sulfamoyl]-benzamide; 4-(bis-pyridin-3-ylmethyl-sulfamoyl)-N-cyclopropylmethoxy-2-(4-ido-phenylamino)-benzamide; N-cyclopropylmethoxy-2-(4-ido-phenylamino)-benzamide; N-cyclopropylmethoxy-4-[(2-hydroxy-ethyl)-pyridin-4-ylmethyl-sulfamoyl]-2-(4-ido-phenylamino)-benzamide; N-cyclopropylmethoxy-2-(4-ido-phenylamino)-4-(methyl-pyridin-3-ylmethyl-sulfamoyl)-benzamide; N-cyclopropylmethoxy-4-[(3-diethylamino-propyl)-pyridin-3-ylmethyl-sulfamoyl]-2-(4-ido-phenylamino)-benzamide; N-cyclopropylmethoxy-2-(4-ido-2-

methyl-phenylamino)-4-phenylsulfamoyl-benzamide; N-cyclopropylmethoxy-2-(4-ido-2-methyl-phenylamino)-4-(pyridin-3-ylsulfamoyl)-benzamide; N-cyclopropylmethoxy-2-(4-ido-2-methyl-phenylamino)-4-[(pyridin-3-ylmethyl)sulfamoyl]-benzamide; 4-(bis-pyridin-3-ylmethyl-sulfamoyl)-N-

5 cyclopropylmethoxy-2-(4-ido-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-4-[(2-hydroxy-ethyl)-pyridin-4-ylmethyl-sulfamoyl]-2-(4-ido-2-methyl-phenylamino)-benzamide; N-cyclopropylmethoxy-2-(4-ido-2-methyl-phenylamino)-4-(methyl-pyridin-3-ylmethyl-sulfamoyl)-benzamide; N-cyclopropylmethoxy-4-[(3-diethylamino-propyl)-pyridin-3-ylmethyl-sulfamoyl]-

10 2-(4-ido-2-methyl-phenylamino)-benzamide; 2-(2-chloro-4-iodo-phenylamino)-N-cyclopropylmethoxy-4-phenylsulfamoyl-benzamide; 2-(2-chloro-4-ido-phenylamino)-N-cyclopropylmethoxy-4-(pyridin-3-ylsulfamoyl)-benzamide; 2-(2-chloro-4-ido-phenylamino)-N-cyclopropylmethoxy-4-[(pyridin-3-ylmethyl)sulfamoyl]-benzamide; 4-(bis-pyridin-3-ylmethyl-

15 sulfamoyl)-2-(2-chloro-4-ido-phenylamino)-N-cyclopropylmethoxy-benzamide; 2-(2-chloro-4-ido-phenylamino)-N-cyclopropylmethoxy-4-[(2-hydroxy-ethyl)-pyridin-4-ylmethyl-sulfamoyl]-benzamide; 2-(2-chloro-4-ido-phenylamino)-N-cyclopropylmethoxy-4-(methyl-pyridin-3-ylmethyl-sulfamoyl)-benzamide; 2-(2-chloro-4-ido-phenylamino)-N-cyclopropylmethoxy-4-[(3-

20 diethylamino-propyl)-pyridin-3-ylmethyl-sulfamoyl]-benzamide; and 5-[bis-(4-methoxy-benzyl)sulfamoyl]-2-(2-chloro-4-ido-phenylamino)-3,4-difluoro-benzoic acid; and 2-(2-chloro-4-ido-phenylamino)-5-dimethylsulfamoyl-3,4-difluoro-benzoic acid methyl ester.

25 121. The method of claim 95, wherein said MEK inhibitor has a structure selected from: PD 298458, N-Allyloxy-2-(2-chloro-4-ido-phenylamino)-3,4-difluoro-5-(4-methyl-piperazine-1-sulfonyl)-benzamide; PD 298459, N-Allyloxy-2-(2-chloro-4-ido-phenylamino)-3,4-difluoro-5-(methyl-phenyl-sulfamoyl)-benzamide; PD 298460, 5-(Allyl-methyl-sulfamoyl)-N-

30 allyloxy-2-(2-chloro-4-ido-phenylamino)-3,4-difluoro-benzamide; PD 298463, 1-[5-Allyloxycarbamoyl-4-(2-chloro-4-ido-phenylamino)-2,3-difluorobenzenesulfonyl]-piperidine-3-carboxylic acid amide; PD 298464, N-Allyloxy-

2-(2-chloro-4-iodo-phenylamino)-5-[(3-dimethylamino-propyl)-methyl-sulfamoyl]-3,4-difluoro-benzamide; PD 298465, N-Allyloxy-2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-5-(4-pyridin-2-yl-piperazine-1-sulfonyl)-benzamide; and PD 298467, N-Allyloxy-2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-5-(methoxy-methyl-sulfamoyl)-benzamide.

122. The method of claim 1, wherein said MEK inhibitor has a structure selected from: 2-(2-chloro-4-iodo-phenylamino)-*N*-cyclopropylmethoxy-3,4-difluoro-benzenesulfonamide; and 2-(2-chloro-4-iodo-phenylamino)-cyclopropylmethoxy-3,4-difluoro-benzenesulfonamide.

123. The method of claim 27, wherein said MEK inhibitor has a structure selected from: 2,4-bis-(2-chloro-4-iodo-phenylamino)-3-fluoro-5-nitro-benzoic acid.

124. The method of claim 59, wherein said MEK inhibitor has a structure selected from: 2-(4-ethynyl-2-methyl-phenylamino)-4-fluoro-benzoic acid; and 2-(3',5'-dichloro-biphenyl-4-ylamino)-benzoic acid.

125. The method of claim 95, wherein said MEK inhibitor has a structure selected from: 2-(2-chloro-4-iodo-phenylamino)-*N*-cyclopropylmethoxy-3,4-difluoro-5-sulfamoyl-benzamide; 2-(2-chloro-4-iodo-phenylamino)-3,4-difluoro-*N*-hydroxy-5-sulfamoyl-benzamide; C-(2-chloro-4-iodo-phenylamino)-*N*-cyclopropylmethoxy-dimethylsulfamoyl-difluoro-benzamide; *N*-cyclopropylmethoxy-dimethylsulfamoyl-difluoro-C-(4-iodo-2-methyl-phenylamino)-benzamide; and C-(2-chloro-4-iodo-phenylamino)-difluoro-(methoxy-methyl-sulfamoyl)-*N*-(2-morpholin-4-yl-ethoxy)benzamide.